

What is claimed is:

1. A composition for modulating and/or stimulating the immune system of an animal comprising an oligoribonucleotide (ORN) from bacteria having a molecular weight less than 10kDa.
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2. The composition of claim 1 wherein the oligoribonucleotide (ORN) having a molecular weight less than 10kDa is resistant to hydrolysis by RNase.
- 10 3. The composition of claim 1 wherein the oligoribonucleotides (ORNs) having a molecular weight less than 10kDa occur only in microbes or at frequencies higher than in mammalian cells.
- 15 4. The composition of claim 3 wherein the higher frequencies of oligoribonucleotides (ORNs) occurring in microbes is at least 10 fold more frequent.
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- 20 5. The composition of claim 3 wherein the higher frequencies of ORNs for modulating and/or stimulating the immune system of an animal comprising an oligoribonucleotide (ORN) from bacteria, consisting of a base sequence selected from the group consisting of:
 - SEQ ID NO: 1 (AGAGGGUCGCACGCGGUA),
 - SEQ ID NO: 2 (CGUACUGCAACUCG) or
 - SEQ ID NO: 3 (AGGUACAGCCAGGACUACGA) and a pharmaceutically acceptable carrier or diluent.
- 25 6. The composition of claim 2 wherein the ORN consists of signature sequences as defined in the definitions and found only in microbes as defined in the definitions.
- 30 7. A method for modulating and/or stimulating the immune system of an animal comprising:
 - growing bacteria in a medium;

exposing said bacteria to biological, chemical or physical stress for at least one period of
stress of approximately 10 to 20 minutes separating said medium and
oligoribonucleotides (ORNs) from said bacteria to form a separated product;
filtering said separated product to remove substances having a molecular weight of greater
5 than 10kDa to form a filtrate;
administering said filtrate to said animal, so that the immune system is modulated and/or
stimulated to withstand microbial infections.

8. The method of claim 7 wherein said step exposing said bacteria to biological,
10 chemical or physical stress comprises as many as six repeated washings in pH neutral
buffers thereby inducing the release of H⁺ and ORNs;
separating said medium and oligoribonucleotides (ORNs) from said bacteria to form a
separated product;
filtering said separated product to remove substances having a molecular weight of greater
15 than 10kDa to form a filtrate;
administering individual or combinations of said filtrates to said animal.

9. The method of claim 7 wherein the bacteria are washed in a buffer of pH <5.7 to
remove extraneous material but leave the desired ORNs intact in the cell prior to packaging
20 the bacteria in a neutral pH gel to induce the release of ORNs during storage and shipping
so that upon administration to livestock, the maximum level of ORNs will be administered.

10. The method of claim 8 wherein the bioavailability of nutrients is reduced by
transferring the bacteria from a nutrient-rich media to a non-nutritive media.
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11. The method of claim 10 wherein said non-nutritive media comprises saline at pH
values of 6.0 to 8.0.

12. The method of claim 11 wherein said saline buffer is a phosphate-buffered saline
30 having a pH of about 7.5.

13. The method of claim 7 wherein the bacteria are selected from the group consisting of *Lactobacillus*, *Staphylococcus*, *Streptococcus*, *Pediococcus*, *Pseudomonas*, *Bacillus*, *Escherichia*, *Listeria*, *Enterococcus*, and *Klebsiella*.

5 14. The method of claim 13 wherein the bacteria are selected from the group consisting of *L. acidophilus*, *L. caseii*, *L. fermentum*, *L. plantarum*, *L. monocytogenes*, *L. innocua*, *S. aureus*, *S. typhimurium*, *P. acidolactici*, *B. coryneforme*, *E. coli*, *E. faecium*, *S. pyogenes*, and *K. pneumoniae*.

10 15. The method of claim 7 wherein the bacteria are propagated at a temperature ranging from approximately 22°C to approximately 37°C.

15 16. The method of claim 7 wherein the bacteria are exposed to said biological, chemical or physical stress while they are in their late-growth or stationary phase of their life cycle.

20 17. The method of claim 7 wherein the filtering step includes:
passing said separated product through a 0.22 μm filter to form a sterilized product; and
passing said sterilized product through a filter with a molecular weight cutoff of 10kDa.

18. The method of claim 7 wherein the filtrate containing the oligoribonucleotides (ORNs) with a molecular weight less than 10kDa is administered to an animal selected from the group consisting of humans, poultry and livestock.

25 19. The method of claim 7 wherein the oligoribonucleotides (ORNs) are administered in a concentration of about 1000 to 50,000 AU of said ORNs<10kDa, corresponding to a reading at 254 nm in the UV range of light wherein the concentration of the oligoribonucleotides gives an Optical Density of 1 to 50, or 120 $\mu\text{g}/\text{kg}$ of the animal's body weight.

30 20. The method of claim 7 wherein the oligoribonucleotides are administered in a manner selected from the group consisting of orally, topically, and parenterally.

21. The method of claim 7 wherein the animal is administered the oligoribonucleotides (ORNs) having a weight of between 0.5 and 3 kDa.
22. The method of claim 7 wherein the oligoribonucleotides (ORNs) are administered
5 as an adjuvant for oral or parenteral vaccines.
23. The method of claim 7 wherein the bacteria are exposed to a series of washings
wherein each washing is approximately 10-20 minutes.

10 24. The method of claim 23 wherein the bacteria is exposed to as many as six sequential periods of stress.

25. A method for modulating and/or stimulating the immune system of an animal comprising:

15 (a) preparing an immunopotentiating composition having the ability to stimulate an immune response which composition comprises a mixture of oligoribonucleotides (ORNs) with a molecular weight less than 10 kDa;

(b) combining the composition in a pharmaceutically acceptable carrier; and

(c) administering the resulting composition to said animal in an amount effective to
20 stimulate an immune response so that the immune system of the animal is activated for suppressing microbial infections and the onset of endotoxic shock.

26. The method of claim 25 wherein said mixture of oligoribonucleotides (ORNs) that are resistant to further hydrolysis by ribonuclease are selected from the group consisting of
25 double stranded oligoribonucleotides, substituted oligoribonucleotides and free uracil.

27. The method of claim 25 wherein the composition is administered orally or parenterally at a dose of approximately 0.1 to 1 mg per kg of body weight.

30 28. The method of claim 25 wherein the composition is fed to said animal 36 to 96 hours before a pathogenic challenge.

29. The method of claim 25 wherein the composition is injected into said animal least 36 to 96 hours before a pathogenic challenge.
30. The method of claim 25 wherein the composition is applied topically onto said animal at 36 to 96 hours before a pathogenic challenge.
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31. The method of claim 25 wherein said composition is fed to said animal as a food supplement.
- 10 32. The method of claim 25 wherein said composition is fed to said animal in a tablet or gel twice a week.